

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes
5 a protein comprising the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 24, 26,
28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, or 60.
2. An isolated nucleic acid molecule which encodes an F-box protein, or a fragment
thereof, having a nucleotide sequence that:
 - 10 a) hybridizes under highly stringent conditions to the nucleotide
sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13; and
 - b) does not encompass the nucleotide sequences which encode the
following known F-box proteins: Cdc4, Grr1, Met30, Skp2, Cyclin F,
Elongin A or mouse Md6.
- 15 3. An isolated nucleic acid sequence derived from a mammalian genome that:
 - a) hybridizes under highly stringent conditions to the nucleotide
sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13; and
 - 20 b) encodes a gene product which contains an F-box motif and binds to
Skp1.
4. An isolated nucleic acid molecule which encodes an F-box protein, said nucleic acid
molecule having a nucleotide sequence of SEQ ID NO: 23, 25, 27, 29, 31, 33, 35, 37, 39,
41, 43, 45, 47, 49, 51, 53, 55, 57, or 59.
- 25 5. A nucleotide vector containing the nucleotide sequence of Claim 1, 2, 3, or 4.
6. An expression vector containing the nucleotide sequence of Claim 1, 2, 3, or 4 in
operative association with a nucleotide regulatory sequence that controls expression of the
30 nucleotide sequence in a host cell.
7. A genetically engineered host cell that contains the nucleotide sequence of Claim 1,
2, 3, or 4 in operative association with a nucleotide regulatory sequence that controls
expression of the nucleotide sequence in the host cell.

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8. A transgenic animal having cells which harbor a transgene comprising the nucleic acid of Claim 1, 2, 3, or 4.
9. An animal inactivated in the loci comprising the nucleotide sequence of Claim 1, 2, 3, or 4.
10. An isolated F-box protein having the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, or 60.
11. An antibody that immunospecifically binds the polypeptide of Claim 10.
12. A method of diagnosing proliferative and differentiative related disorders comprising measuring FBP gene expression in a patient sample.
13. A method for screening compounds useful for the treatment of proliferative and differentiative disorders comprising contacting a compound with a cell expressing an F-box protein having the amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, or 60, or a fragment thereof, and its substrate, and detecting a change in the F-box protein activity.
14. The method of Claim 13 wherein the change in the F-box protein activity is detected by detecting a change in the interaction of the F-box protein with one or more proteins.
15. The method of Claim 14 in which one of the one or more proteins is the substrate of the F-box protein.
16. The method of Claim 13 in which at least one of the one or more proteins is a component of the ubiquitin pathway.
17. The method of Claim 13 in which one of the one or more proteins is Skp1.
18. The method of Claim 13 in which the F-box protein is Fbp1 and the substrate is β -catenin or IKB α .
19. The method of Claim 13 wherein the change in the F-box protein activity is detected by detecting a change in the ubiquitination or degradation of the substrate.

20. A method for screening compounds useful for the treatment of proliferative and differentiative disorders comprising contacting a compound with a cell or a cell extract expressing Skp2 and one or both of p27 and E2F, and detecting a change in the activity of Skp2.
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21. The method of Claim 20 wherein the change in the activity of Skp2 is detected by detecting a change in the interaction of Skp2 with either p27 or E2F-1.
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22. The method of Claim 20 wherein the change in the activity of Skp2 is detected by detecting a change in the ubiquitination or degradation of p27 or E2F-1.
23. A method for treating a proliferative or differentiative disorder in a mammal comprising administering to the mammal a compound to the mammal that modulates the
- 15 synthesis, expression or activity of an FBP gene or gene product so that symptoms of the disorder are ameliorated.
24. The method of Claim 23 in which the disorder is breast cancer.
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25. The method of Claim 23 in which the disorder is ovarian cancer.
26. The method of Claim 23 in which the disorder is prostate cancer.
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27. The method of Claim 23 in which the disorder is small cell lung carcinoma.

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